

Section II (Remarks)

A. Summary of Amendment to the Claims

By the present Amendment, claims 1, 5, 7 and 8 have been amended. No new matter within the meaning of 35 U.S.C. §132(a) has been introduced by the foregoing amendments.

The amendments made herein are fully consistent with and supported by the originally-filed disclosure of this application.

In claim 1 the phrase “and one or more mitogenically stimulated surface markers” has added to the preamble. This language is supported by original claim 1, as filed. Additionally in claim 1, steps (a) to (c) have been clarified, wherein (a) refers to obtaining a sample, (b) refers to the quantification of the cells bearing the surface marker before stimulation and (c) refers to the stimulation. This sequence of steps is supported in the specification at page 2 and pages 7-8. Previous step (c) has been amended to step (e) and has been revised to recite that the stimulation index is calculated as quotient of the number of cells bearing the surface marker before and after stimulation, which is supported at page 8, last sentence of paragraph 1. Additionally, step (f) has been added, reciting that the disease or predisposition to the disease is detected, if the calculated quotient of step (e) is from 10 to 100. Such amendment is supported by the language of the original claims, but has been amended to clarify the original language.

Claim 5 has been amended to depend from claim 2 and to recite that the compounds are added to the sample before step (b) which is supported by the working example on page 7, last paragraph of the specification.

Claims 7 and 8 have been amended in accordance with the new numbering of the steps of claim 1.

Thus, upon entry of the amendments, claims 1-13 will be pending, of which claims 9-13 are withdrawn.

B. Rejection of the Claims under 35 U.S.C. § 112

Definiteness

In the Office Action mailed July 31, 2009, the examiner has rejected claims 1-8 as indefinite. Applicants respectfully traverse the rejection.

Specifically, claim 1 is rejected for recitation of the phrase “mitogenically stimulated cells...before and after step (a).” The examiner’s attention is respectfully drawn to claim 1, as amended, where the rejected phrase is no longer present within the claims and the claim now recites mitogenic stimulation of the cell population in step (c) and quantification of the cells within the mitogenically stimulated cell population after step (c). It is respectfully submitted that, as amended, the steps of claim 1 are clear.

Additionally, claim 1 is rejected as “omitting essential steps...steps leading to a quantification of surface markers before stimulation and steps leading to a determination of the number of cells bearing the surface marker before stimulation.” (Office Action mailed July 31, 2008, p. 3.) It is respectfully submitted that claim 1, as amended, is clear. Specifically, amended claim 1 contains method steps (a)-(f), where step (b) provides for quantification of the cells bearing the surface marker before stimulation and step (d) provides for quantification of the cells after stimulation. As amended, claim 1 meets the definiteness requirements of 35 U.S.C. §112, second paragraph.

In the Office Action mailed July 31, 2008, claim 5 is rejected as being incomplete for omitting essential elements and for improperly limiting claim 1. The examiner’s attention is respectfully drawn to amended claim 5, where the language of the claim has been amended. As amended, claim 5 depends from claim 2, which properly limits step (a) of claim 1. Claim 5 further limits step (a) of claim 1. As amended, claim 5 meets the definiteness requirements of 35 U.S.C. §112, second paragraph.

Since all of the examiner’s rejections under 35 U.S.C. § 112, second paragraph have been addressed, it is respectfully submitted that all of claims 1-8 pending and under examination meet the definiteness requirements of 35 U.S.C. §112, second paragraph.

C. Rejection of the Claims under 35 U.S.C. § 102

In the Office Action mailed July 31, 2008, the examiner has rejected claims 1-4 and 6 under 35 U.S.C. §102(b) as anticipated by Neubert et al., Teratogenesis, Carcinogenesis and Mutagenesis.

20:171-193 (2000) (hereinafter “Neubert et al.”). Applicants respectfully disagree and traverse the rejection.

The examiner’s attention is respectfully drawn to claim 1, as amended, from which claims 2-4 and 6 all depend. Amended claim 1 recites a method of diagnosing Alzheimer’s disease or an early stage of Alzheimer’s disease or a predisposition for Alzheimer’s disease, wherein the diagnosis is based upon calculation of a stimulation index as a quotient of the cells bearing a surface marker before and after mitogenic stimulation, where a positive diagnosis is made when a stimulation index of 10-100 is calculated. All claims dependent from claim 1 are also limited by the recitation of claim 1.

It is well established that a claim preamble may be limiting to a claim. See MPEP 2111.02. “‘If the claim preamble, when read in the context of the entire claim, recites limitations of the claim, or, if the claim preamble is ‘necessary to give life, meaning, and vitality’ to the claim, then the claim preamble should be construed as if in the balance of the claim.’ *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165-66 (Fed. Cir. 1999). See also *Jansen v. Rexall Sundown, Inc.*, 342 F.3d 1329, 1333, 68 USPQ2d 1154, 1158 (Fed. Cir. 2003).”

In claim 1 of the present application, the preamble recites “a method of diagnosing Alzheimer’s disease or an early stage of or a predisposition for this disease...” It is respectfully submitted that the preamble of claim 1 should be read “as if in the balance of the claim.” Indeed, the balance of the claim contains in step (f) a recitation “that the sample is from a patient suffering from Alzheimer’s disease or an early stage of or a predisposition for this disease...” Furthermore, as the title suggests, the entire application is directed to “QUICK TEST FOR THE DIAGNOSIS OF ALZHEIMER’S DISEASE.” Clearly applicants claim a method of diagnosing Alzheimer’s disease.

By the examiner’s admission, Neubert et al “makes no mention of the method within the context of diagnosis of Alzheimer’s disease...” (Office Action mailed July 31, 2008, p. 5.) While the examiner alleges that the preamble of claim 1 is non-limiting, applicants respectfully disagree, as set forth above.

Neubert et al. does not teach or disclose a method of diagnosing Alzheimer's disease. Neubert et al. does not disclose a method wherein Alzheimer's disease is detected if a stimulation index of 10 to 100 is calculated as a quotient of the cells bearing a surface marker before and after mitogenic stimulation. Therefore, Neubert et al. does not anticipate claim 1, or claims 2-4 or 6, dependent therefrom. Withdrawal of the rejection is respectfully requested.

Additionally, claims 1-6 and 8 are rejected under 35 U.S.C. §102 as anticipated by Stieler et al., NeuroReport, 12(18): 3869-3972 (December 21, 2001) (hereinafter "Stieler et al."). Applicants respectfully disagree and traverse the rejection.

As set forth in detail above, claim 1, and all claims dependent therefrom, are directed to a method of diagnosing Alzheimer's disease or an early stage of Alzheimer's disease or a predisposition for Alzheimer's disease, wherein the diagnosis is based upon calculation of a stimulation index as a quotient of the cells bearing a surface marker before and after mitogenic stimulation, where a positive diagnosis is made when a stimulation index of 10-100 is calculated.

Stieler et al. report the presentation of the CD69 activation marker on lymphocytes of patients with Alzheimer's disease and controls without mental impairment. Stieler et al. does not disclose diagnosis of Alzheimer's disease, as recited in claim 1. The samples used in Stieler et al. are already determined as being from patients with Alzheimer's disease or from healthy subjects.

In describing Stieler et al. the examiner characterizes it as teaching "the effects of mitogenic stimulation as a function of the number of cells bearing the surface marker(s) before and after stimulation (Figure 1)." (Office Action mailed July 31, 2008, p. 6.) Applicants respectfully disagree with this characterization. Contrary to the examiner's assertion, Stieler et al. define the stimulation index "as the ratio of CD69 expression after mitogenic stimulation to unstimulated control." (Stieler, p. 3970, 1st col.) Therefore, Stieler et al. does not disclose calculation of the stimulation index as the quotient of the number of cells bearing the surface marker before and after simulation as claimed. Furthermore, Stieler et al. does not disclose that a stimulation index of 10 to 100 is indicative of Alzheimer's disease. Therefore, Stieler et al. does not anticipate claim 1 as amended.

Since Stieler et al. does not describe a stimulation index as set forth in claim 1 and claims, Stieler et al. does not anticipate the claimed invention. Accordingly, withdrawal of the rejection of

claims 1-6 and 8 under 35 U.S.C. § 102(b) as being anticipated by Stieler et al. is respectfully requested.

D. Rejection of the Claims under 35 U.S.C. § 103

In the Office Action mailed July 31, 2008, the examiner has rejected claim 7 under 35 U.S.C. § 103 as obvious over Stieler et al. in view of Rasmussen, et al., *J. Immunol. Meth.*, 146(2): 195-202 (2002) (hereinafter “Rasmussen et al.”). Applicants respectfully disagree and traverse the rejection.

Claim 7 recites a method, wherein immunomagnetic separation is applied in a diagnosis of Alzheimer’s disease which is detected if a stimulation index of 10 to 100 is calculated as a quotient of the cells bearing a surface marker before and after mitogenic stimulation. Claim 7 depends from claim 1 and, though claim 1 is not rejected under 35 U.S.C. § 103, as a dependent claim, claim 7 inherently contains all elements of claim 1.

As set forth above, Stieler et al. does not anticipate the method of claim 1, as Stieler et al. does not disclose calculation of the stimulation index as the quotient of the number of cells bearing the surface marker before and after simulation as claimed, nor does Stieler et al. disclose that a stimulation index of 10 to 100 is indicative of Alzheimer’s disease. Therefore, Stieler et al. does not anticipate claim 1 as amended. Citation of Rasmussen et al. in combination with Stieler et al. as anticipating claim 7 does not remedy this deficiency in anticipation of claim 1. Claim 7 recites the method of claim 1, wherein “the antibodies in step (d) are bound to magnetic particles and the separation is carried out via immunomagnetic separation.”

The combination of Stieler et al. and Rasmussen et al. still does not provide a method where calculation of the stimulation index as the quotient of the number of cells bearing the surface marker before and after simulation as claimed, and where a stimulation index of 10 to 100 is indicative of Alzheimer’s disease. Therefore, it would not have been obvious at the time of filing of the present application, in view of the combined teachings of Stieler et al. and Rasmussen et al. to separate cells bearing the surface markers from cells not bearing the surface marker by immunomagnetic separation and to detect Alzheimer’s disease when a stimulation index of 10 to 100 is calculated as a quotient of the cells bearing a surface marker before and after mitogenic stimulation.

As Stieler et al. in light of Rasmussen et al. does not provide any logical basis for the method recited in claim 7, Stieler et al. in light of Rasmussen et al. does not render the claimed invention obvious. Accordingly, withdrawal of the rejection of claim 7 under 35 U.S.C. § 103 (a) as being obvious over Stieler et al. in light of Rasmussen et al. is respectfully requested.

CONCLUSION

Based on the foregoing, all of Applicants' pending claims 1-8 are patentably distinguished over the art, and in form and condition for allowance. The examiner is requested to favorably consider the foregoing, and to responsively issue a Notice of Allowance. If any issues require further resolution, the examiner is requested to contact the undersigned attorney at (919) 419-9350 to discuss same.

Respectfully submitted,

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/steven j. hultquist/
Steven J. Hultquist
Reg. No. 28,021
Attorney for Applicants

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/kelly k. reynolds/
Kelly K. Reynolds
Reg. No. 51,154
Attorney for Applicants

INTELLECTUAL PROPERTY/
TECHNOLOGY LAW
Phone: (919) 419-9350
Fax: (919) 419-9354
Attorney File No.: 4121-180

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